

## AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

Claims 1-52 (Canceled).

53. (Previously Presented) A computer system for determining a level of protein activity comprising a processor and a memory coupled to said processor, said memory encoding one or more programs, said one or more programs causing said processor to perform a method comprising determining a level of perturbation to said protein at which similarity is greatest between a diagnostic profile and a perturbation response profile extracted from perturbation response curves for said determined level of perturbation to said protein, said diagnostic profile having been obtained by a method comprising measuring a first plurality of cellular constituents in a cell of said cell type, said perturbation response curves being the products of a method comprising:

(i) providing perturbation response profiles of said protein for said cell type, wherein said perturbation response profiles are obtained by measuring a second plurality of cellular constituents in a cell of said cell type at a plurality of discrete levels of perturbation to said protein, and

(ii) interpolating said perturbation response profiles so that a perturbation response profile may be extracted over a range of levels of perturbation to said protein, wherein said interpolated response profiles comprise said perturbation response curves,

wherein said determined level of perturbation to said protein represents said protein activity level in said cell type.

54. (Previously Presented) The computer system of claim 53 wherein determining the level of perturbation is achieved by a method comprising:

(a) determining the value of a function of the difference between said diagnostic profile and the perturbation response profile extracted from said perturbation response curves for a level of perturbation to said protein; and

(b) minimizing said determined value of said function by varying the level of perturbation to said protein to determine a level of perturbation that minimizes said determined value of said function.

55. (Previously Presented) The computer system of claim 53 wherein said diagnostic profiles and said perturbation response curves are made available in said memory.

56. (Previously Presented) The computer system of claim 55 wherein said programs cause said processor to perform said step of interpolating said perturbation response profiles.

57. (Previously Presented) The computer system of claim 54 wherein said function comprises a sum of the squares of differences of the diagnostic profile and the perturbation response profile extracted from said perturbation response curves.

58. (Previously Presented) The computer system of claim 53 wherein determining the level of perturbation is achieved by a method comprising:

(a) determining the value of a function of the correlation between said diagnostic profile and the perturbation response profile extracted from said perturbation response curves for a level of perturbation to said protein; and

(b) maximizing said determined value of said function by varying the level of perturbation to said protein to determine a level of perturbation that maximizes said determined value of said function.

59. (Previously Presented) The computer system of claim 54 wherein said minimizing comprises performing the Levenberg-Marquandt method.

Claims 60-66 (Canceled).

67. (Previously Presented) A computer system for determining levels of protein activity comprising a processor and a memory coupled to said processor, said memory encoding one or more programs, said one or more programs causing said processor to perform a method comprising determining a level of perturbation to each said protein at which similarity is greatest between a diagnostic profile and a combination of perturbation response profiles extracted from perturbation response curves for each said protein for each said determined level of perturbation, said diagnostic profile having been obtained by a

method comprising measuring a first plurality of cellular constituents in a cell of said cell type, wherein said perturbation response curves for each of said proteins are the products of a method comprising

(i) providing perturbation response profiles of said protein for said cell type, wherein said perturbation response profiles are obtained by measuring a second plurality of cellular constituents in a cell of said cell type at a plurality of discrete levels of perturbation to said protein, and

(ii) interpolating said perturbation response profiles so that a perturbation response profile may be extracted over a range of levels of perturbation to said protein, wherein said interpolated response profiles comprise said perturbation response curves

wherein said determined level of perturbation to each said protein represents said activity level of each said protein in said cell type.

68. (Previously Presented) The computer system of claim 67 wherein said determining the level of perturbation is achieved by a method comprising:

(a) determining the value of a function of the difference between said diagnostic profile and the combination of the perturbation response profiles extracted from said perturbation response curves for said level of perturbation to each said protein; and

(b) minimizing said determined value of said function by varying the level of perturbation to each said protein to determine the level of perturbation to each said protein that minimizes said determined value of said function.

Claims 69-70 (Canceled).

71. (Previously Presented) A computer system for determining a level of activity of a biologically active cellular constituent of interest comprising a processor and a memory coupled to said processor, said memory encoding one or more programs, said one or more programs causing said processor to perform a method comprising determining a level of perturbation to the cellular constituent of interest at which similarity is greatest between a diagnostic profile and a perturbation response profile extracted from perturbation response curves for said determined level of perturbation to the cellular constituent of interest,

said diagnostic profile having been obtained by a method comprising measuring a first plurality of cellular constituents in a cell of said cell type, said perturbation response curves being the products of a method comprising:

- (i) providing perturbation response profiles of the cellular constituent of interest for said cell type, wherein said perturbation response profiles are obtained by measuring a second plurality of cellular constituents in a cell of said cell type at a plurality of discrete levels of perturbation to the cellular constituent of interest, and
- (ii) interpolating said perturbation response profiles so that a perturbation response profile may be extracted over a range of levels of perturbation to the cellular constituent of interest, wherein said interpolated response profiles comprise said perturbation response curves,

wherein said determined level of perturbation to the cellular constituent of interest represents the activity level of said cellular constituent of interest in said cell type.

72. (Previously Presented) The computer system of claim 71, wherein determining the level of perturbation is achieved by a method comprising:

- (a) determining the value of a function of the difference between said diagnostic profile and the perturbation response profile extracted from said perturbation response curves for a level of perturbation to said cellular constituent of interest; and
- (b) minimizing said determined value of said function by varying the level of perturbation to said cellular constituent of interest to determine a level of perturbation that minimizes said determined value of said function.

Claims 73-78 (Canceled).

79. (Previously Presented) A computer program product for use in conjunction with a computer having a processor and a memory connected to the processor, said computer program product comprising a computer readable storage medium having a computer program mechanism encoded thereon, wherein said computer program mechanism may be loaded into the memory of said computer and cause said computer to carry out a method comprising determining a level of perturbation to a protein at which similarity is greatest

between a diagnostic profile and a perturbation response profile extracted from perturbation response curves for said determined level of perturbation to a protein, said diagnostic profile having been obtained by a method comprising measuring a first plurality of cellular constituents in a cell of said cell type, said perturbation response curves being the products of a method comprising:

- (i) providing perturbation response profiles of said protein for said cell type, wherein said perturbation response profiles are obtained by measuring a second plurality of cellular constituents in a cell of said cell type at a plurality of discrete levels of perturbation to said protein, and

- (ii) interpolating said perturbation response profiles so that a perturbation response profile may be extracted over a range of levels of perturbation to said protein, wherein said interpolated response profiles comprise said perturbation response curves,

wherein said determined level of perturbation to said protein represents a level of activity of said protein in said cell type.

80. (Previously Presented) A computer program product for use in conjunction with a computer having a processor and a memory connected to the processor, said computer program product comprising a computer readable storage medium having a computer program mechanism encoded thereon, wherein said computer program mechanism may be loaded into the memory of said computer and cause said computer to carry out a method comprising determining an activity level of a protein in a cell treated with a drug according to a method comprising determining a level of perturbation to said protein at which similarity is greatest between a diagnostic profile and a perturbation response profile extracted from perturbation response curves for the determined level of perturbation to said protein, wherein:

- (a) the diagnostic profile is obtained by a method comprising measuring a first plurality of cellular constituents in the cell treated with said drug; and

- (b) the perturbation response curves are provided by a method comprising

- (i) providing perturbation response profiles of said protein for a cell, wherein said perturbation response profiles are obtained by a method

comprising measuring a second plurality of cellular constituents in a cell at a plurality of discrete levels of perturbation to said protein,

- (ii) interpolating said perturbation response profiles so that a perturbation response profile may be extracted over a range of levels of perturbation to said protein, wherein said interpolated response profiles comprise said perturbation response curves,

and wherein said determined level of perturbation to said protein represents said protein activity level in said cell treated with said drug and said protein activity level is a measure of activity of said drug.

81. (Previously Presented) A computer program product for use in conjunction with a computer having a processor and a memory connected to the processor, said computer program product comprising a computer readable storage medium having a computer program mechanism encoded thereon, wherein said computer program mechanism may be loaded into the memory of said computer and cause said computer to carry out a method comprising determining a level of perturbation to a biologically active cellular constituent of interest at which similarity is greatest between a diagnostic profile and a perturbation response profile extracted from perturbation response curves for said determined level of perturbation to the cellular constituent of interest, said diagnostic profile having been obtained by a method comprising measuring a first plurality of cellular constituents in a cell of said cell type, said perturbation response curves being the products of a method comprising:

- (i) providing perturbation response profiles of the cellular constituent of interest for said cell type, wherein said perturbation response profiles are obtained by measuring a second plurality of cellular constituents in a cell of said cell type at a plurality of discrete levels of perturbation to the cellular constituent of interest, and
- (ii) interpolating said perturbation response profiles so that a perturbation response profile may be extracted over a range of levels of perturbation to the cellular constituent of interest, wherein said interpolated response profiles comprise said perturbation response curves,

wherein said determined level of perturbation to the cellular constituent of interest represents a level of activity of said cellular constituent of interest in said cell type.

Claims 82-84 (Canceled).